STIC-ILL

From: Gambel, Phillip
Sent: Thursday, January 08, 2004 12:14 PM
To: STIC-ILL
Subject: anti-tnf or anti-ifn hiv / aids

stic

please provide the following references to

phillip gambela
r tunit 1644
308-3997

1644 mailbox 9e12

thanx

----------anti-tnf or anti-ifn hiv / aids ----------

3/7/8 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08315013 95002983 PMID: 7522637
Cross-linking of CD4 molecules upregulates Fas antigen expression in lymphocytes by inducing interferon-gamma and tumor necrosis factor-alpha secretion.
Oyaizu N; McCloskey T W; Than S; Hu R; Kalyanaraman V S; Pahwa S
Department of Pediatrics, North Shore University Hospital-Cornell University Medical College, Manhasset, NY.
Blood (UNITED STATES) Oct 15 1994, 84 (8) p2622-31, ISSN 0006-4971 Journal Code: 7603509
Contract/Grant No.: AI28281; AI; NIAID; DA05061; DA; NIDA; HD26606; HD; NICHD
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We have recently shown that, in unfractioned peripheral blood mononuclear cells (PBMCs), the cross-linking of CD4 molecules (CD4XL) is sufficient to induce T-cell apoptosis. However, the underlying mechanism for the CD4XL-mediated T-cell apoptosis is largely unknown. Several recent studies have shown that Fas antigen (Ag), a cell-surface molecule, mediates apoptosis-triggering signals. We show here that cross-linking of CD4 molecules, induced either by anti-CD4 monoclonal antibody (MoAb) Leu3a or by human immunodeficiency virus-1 (HIV-1) envelope protein gp160, upregulates Fas Ag expression as well as Fas mRNA in normal lymphocytes. Addition of the tyrosine protein kinase inhibitor genistein or of the immunosuppressive agent cyclosporin A abrogated these effects. The upregulation of Fas Ag closely correlated with apoptotic cell death, as determined by flow cytometry. In addition, CD4XL resulted in the induction of interferon-gamma (IFN-gamma) and tumor necrosis factor-alpha (TNF-alpha) in the absence of interleukin-2 (IL-2) and IL-4 secretion in PBMCs. Both INF-gamma and TNF-alpha were found to contribute to Fas Ag upregulation and both anti-IFN-gamma and anti-TNF-alpha antibodies blocked CD4XL-induced Fas Ag upregulation and lymphocyte apoptosis. These findings strongly suggest that aberrant cytokine secretion induced by CD4XL and consequent upregulation of Fas Ag expression might play a critical role in triggering peripheral T-cell apoptosis and thereby contribute to HIV disease pathogenesis.

```
TEM:OS  - DIALOG OneSearch
  File   5:Biosis Previews(R)  1969-2003/Dec W2
         (c) 2003 BIOSIS
  File  73:EMBASE  1974-2003/Dec W1
         (c) 2003 Elsevier Science B.V.
  File 155:MEDLINE(R)  1966-2003/Nov W4
         (c) format only 2003 The Dialog Corp.
*File 155: Medline has temporarily stopped updating (12-2003). And for
notice of corrected dosage, please see HELP NEWS 154.
  File 399:CA SEARCH(R)  1967-2003/UD=13926
         (c) 2003 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
Alert feature enhanced for multiple files, etc. See HELP ALERT.

      Set  Items  Description
      ---  -----  -----------
? e au=skurkovich ?
```

```
Set     Items   Description
S1         58   E2-E7
S2         37   RD S1 (unique items)
S3         10   S2 AND (HIV OR AIDS)
S4         10   RD S3 (unique items)
S5        208   (INTERFERON$ OR TNF$ OR TUMOUR(W)NECROSIS OR TUMOR(W)NECRO-
              SIS)(20N)(ANTIBOD?) AND (TREAT? OR INHIBIT? OR PREVENT? OR SU-
              PPRESS? OR THERAP?)(10N)(AIDS OR HIV?)
S6        151   RD S5 (unique items)
?
```

```
ds

Set     Items   Description
S1         58   E2-E7
S2         37   RD S1 (unique items)
S3         10   S2 AND (HIV OR AIDS)
S4         10   RD S3 (unique items)
S5        208   (INTERFERON$ OR TNF$ OR TUMOUR(W)NECROSIS OR TUMOR(W)NECRO-
              SIS)(20N)(ANTIBOD?) AND (TREAT? OR INHIBIT? OR PREVENT? OR SU-
              PPRESS? OR THERAP?)(10N)(AIDS OR HIV?)
S6        151   RD S5 (unique items)
S7        105   (CYTOKINE$ OR INTERFERON$ OR TNF$ OR TUMOUR(W)NECROSIS OR -
              TUMOR(W)NECROSIS)(10N)(ANTIBOD?) AND (ANTIBOD?)(20N)(TREAT? OR
               THERAP? OR PREVENT? OR SUPPRESS? OR INHIBIT?)(10N)(AIDS OR H-
              IV?)
S8         75   RD S7 (unique items)
?
```

```
  ---  -----  -----------
? e au=skurkovich ?

Ref    Items  Index-term
E1         1  AU=SKURKOVA, D.
E2         1  AU=SKURKOVIC B
E3         0 *AU=SKURKOVICH ?
E4        33  AU=SKURKOVICH B
E5         4  AU=SKURKOVICH B S
E6        13  AU=SKURKOVICH B.
E7         7  AU=SKURKOVICH BORIS
E8         3  AU=SKURKOVICH G
E9         1  AU=SKURKOVICH G P
E10       28  AU=SKURKOVICH G V
E11        1  AU=SKURKOVICH G.V.
E12       28  AU=SKURKOVICH S

          Enter P or PAGE for more
? s e2-e7
                1  AU=SKURKOVIC B
                0  AU=SKURKOVICH ?
               33  AU=SKURKOVICH B
                4  AU=SKURKOVICH B S
               13  AU=SKURKOVICH B.
                7  AU=SKURKOVICH BORIS
      S1       58  E2-E7
? rd s1
...examined 50 records  (50)
...completed examining records
      S2       37  RD S1 (unique items)
? s s2 and (hiv or aids)
               37  S2
           368177  HIV
           263715  AIDS
      S3       10  S2 AND (HIV OR AIDS)
? rd s3
...completed examining records
      S4       10  RD S3 (unique items)
? t s4/3/all

 4/3/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

0014081449   BIOSIS NO.: 200300050168
Anticytokine therapy: New approach to the treatment of autoimmune and
  cytokine-disturbance diseases.
AUTHOR: Skurkovich S V (Reprint); Skurkovich B; Kelly J A
AUTHOR ADDRESS: Advanced Biotherapy Labs, 802 Rollins Avenue, Rockville,
  MD, 20852, USA**USA
AUTHOR E-MAIL ADDRESS: sskurkovich@erols.com
JOURNAL: Medical Hypotheses  59 (6): p770-780 December 2002 2002
MEDIUM: print
ISSN: 0306-9877 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English


 4/3/2     (Item 2 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

0013521493   BIOSIS NO.: 200200115004
```

Treatment of autoimmune diseases
AUTHOR: **Skurkovich Boris** (Reprint); Skurkovich Simon V
AUTHOR ADDRESS: Pawtucket, RI, USA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1253 (4): Dec. 25, 2001 2001
MEDIUM: e-file
PATENT NUMBER: US 6333032 PATENT DATE GRANTED: December 25, 2001 20011225
PATENT CLASSIFICATION: 424-1301 PATENT ASSIGNEE: Advanced Biotherapy Concepts, Inc., Carlsbad, CA, USA PATENT COUNTRY: USA
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

4/3/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013471655 BIOSIS NO.: 200200065166
Treatment of autoimmune diseases, including **AIDS**, by removel of interferons, TNFS and receptors therefor
AUTHOR: Skurkovich S V; **Skurkovich B**
AUTHOR ADDRESS: Rockville, Md., USA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1198 (1): p331 May 6, 1997 1997
MEDIUM: print
PATENT NUMBER: US 5626843 PATENT DATE GRANTED: May 6, 1997 19970506
PATENT CLASSIFICATION: 424-140.1 PATENT ASSIGNEE: ADVANCED BIOTHERAPY CONCEPTS, INC. PATENT COUNTRY: USA
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Citation
LANGUAGE: English

4/3/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011916647 BIOSIS NO.: 199900176307
Treatment of autoimmune diseases, including **AIDS**
AUTHOR: **Skurkovich B**; Skurkovich S V
AUTHOR ADDRESS: Pawtucket, R.I., USA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1220 (5): p4456 March 30, 1999 1999
MEDIUM: print
PATENT NUMBER: US 5888511 PATENT DATE GRANTED: March 30, 1999 19990330
PATENT CLASSIFICATION: 424-145.1 PATENT ASSIGNEE: ADVANCED BIOTHERAPY CONCEPTS, INC. PATENT COUNTRY: USA
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Citation
LANGUAGE: English

4/3/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009249951 BIOSIS NO.: 199497271236
A disturbance of interferon synthesis with the hyperproduction of unusual kinds of interferon can trigger autoimmune disease and play a pathogenetic role in **AIDS**: The removal of these interferons can be

therapeutic
AUTHOR: Skurkovich S (Reprint); **Skurkovich B**; Bellanti J A
AUTHOR ADDRESS: 802 Rollins Ave., Rockville, MD 20852, USA**USA
JOURNAL: Medical Hypotheses 42 (1): p27-35 1994 1994
ISSN: 0306-9877
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

4/3/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008960693 BIOSIS NO.: 199396125109
A disturbance of interferon synthesis with the hyperproduction of unusual kinds of interferon can trigger autoimmune disease and play a pathogenetic role in **AIDS**: The removal of these interferons can by therapeutic
AUTHOR: Skurkovich S (Reprint); **Skurkovich B**; Bellanti J A
AUTHOR ADDRESS: Advanced Biotherapy Concepts Lab., Rockville, MD, USA**USA
JOURNAL: Medical Hypotheses 41 (2): p177-185 1993
ISSN: 0306-9877
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008457218 BIOSIS NO.: 199344020114
Aberrant IFN may help **HIV** survive and replicate: Its removal in **AIDS** patients may halt this process and help restore the immune system
AUTHOR: Skurkovich S V (Reprint); **Skurkovich B**
AUTHOR ADDRESS: Adv. Biotherapy Concepts Labs, Rockville, Md., USA**USA
JOURNAL: Journal of Interferon Research 12 (SUPPL. 1): pS118 1992
CONFERENCE/MEETING: Annual Meeting of the International Society for Interferon Research, Toronto, Ontario, Canada, September 28-October 2, 1992. J INTERFERON RES
ISSN: 0197-8357
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: English

4/3/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0006425336 BIOSIS NO.: 198937003085
METHOD FOR TREATING **AIDS** AND OTHER IMMUNE DEFICIENCIES AND IMMUNE DISORDERS US PATENT-4824432. APRIL 25 1989
AUTHOR: SKURKOVICH S (Reprint); **SKURKOVICH B**
AUTHOR ADDRESS: ROCKVILLE, MD, USA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1101 (4): p2532 1989
PATENT NUMBER: US 4824432 PATENT DATE GRANTED: April 25, 1989 19890425
PATENT CLASSIFICATION: 604-4 PATENT ASSIGNEE: SVS LABORATORIES, INC
PATENT COUNTRY: USA
ISSN: 0098-1133
DOCUMENT TYPE: Patent

RECORD TYPE: Citation
LANGUAGE: ENGLISH

4/3/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005702458 BIOSIS NO.: 198784056607
A UNIFYING MODEL OF THE IMMUNOREGULATORY ROLE OF THE INTERFERON SYSTEM CAN INTERFERON PRODUCE DISEASE IN HUMANS?
AUTHOR: SKURKOVICH S (Reprint); **SKURKOVICH B**; BELLANTI J A
AUTHOR ADDRESS: DEP OF INTERNATIONAL CENT FOR INTERDISCIPLINARY STUDIES OF IMMUNOL, GEORGETOWN UNIV SCH OF MED, WASHINGTON, DC 20007, USA**USA
JOURNAL: Clinical Immunology and Immunopathology 43 (3): p362-373 1987
ISSN: 0090-1229
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

4/3/10 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

12013934 EMBASE No: 2003124847
Anti-interferon-gamma antibodies in the treatment of autoimmune diseases
Skurkovich B.; Skurkovich S.
S. Skurkovich, Advanced Biotherapy Inc., 802 Rollins Ave, Rockville, MD 20852 United States
AUTHOR EMAIL: sskurkovich@erols.com
Current Opinion in Molecular Therapeutics (CURR. OPIN. MOL. THER.) (United Kingdom) 2003, 5/1 (52-57)
CODEN: CUOTF ISSN: 1464-8431
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 52
? t s4/7/all

0005702458 BIOSIS NO.: 198784056607
A UNIFYING MODEL OF THE IMMUNOREGULATORY ROLE OF THE INTERFERON SYSTEM CAN INTERFERON PRODUCE DISEASE IN HUMANS?
AUTHOR: SKURKOVICH S (Reprint); SKURKOVICH B; BELLANTI J A
AUTHOR ADDRESS: DEP OF INTERNATIONAL CENT FOR INTERDISCIPLINARY STUDIES OF IMMUNOL, GEORGETOWN UNIV SCH OF MED, WASHINGTON, DC 20007, USA**USA
JOURNAL: Clinical Immunology and Immunopathology 43 (3): p362-373 1987
ISSN: 0090-1229
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: This hypothesis is a presentation of a unifying model of the interferon (IFN) system as a cascade of sequentially interacting responses of IFNs-.alpha., -.beta., and -.gamma. involved in modulation of the immune response. We propose that every antigen is an IFNogen. The first stage(s) of immune responsiveness is associated primarily with the production of the family of IFN-.alpha.. In certain immunologically mediated diseases, including the autoimmune diseases and AIDS, disturbances in the synthesis of IFN-.alpha. occur with a switch to the production of predominantly acid-labile types, which have a negative immunoregulatory effect. Moreover, disturbances of IFN synthesis in the embryo or fetus can lead to deformities. Some viruses and other biological and chemical substances manifest a pathological effect by the IFN they induce. This IFN may help sustain the viruses and other substances which induce this IFN. We think it is unsafe to give patients immunoregulators in incomplete form. Thus, there is a potential danger in giving patients recombinants forms of IFNs and interleukin 2 produced in bacteria. In certain immune disorders, we may be able to treat patients by the binding or removal of hyperproduced IFNs from the body. This may lead to the restoration of immunologic balance and clinical improvement.

skurkovich ----------

4/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008960693 BIOSIS NO.: 199396125109
A disturbance of interferon synthesis with the hyperproduction of unusual kinds of interferon can trigger autoimmune disease and play a pathogenetic role in AIDS: The removal of these interferons can by therapeutic
AUTHOR: Skurkovich S (Reprint); Skurkovich B; Bellanti J A
AUTHOR ADDRESS: Advanced Biotherapy Concepts Lab., Rockville, MD, USA**USA
JOURNAL: Medical Hypotheses 41 (2): p177-185 1993
ISSN: 0306-9877
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Disturbances of interferon synthesis with the hyperproduction of unusual kinds of interferons may be the initial step which triggers autoimmune disease through a concatenation of pathological reactions including the disturbance of several immunological and interferon cascades. This fundamental disturbance can result either from a genetic predisposition or from the influence of certain viruses (or viral particles) or both factors together. The administration of interferons to individuals with an underlying or latent autoimmune condition can exacerbate or trigger the disease. AIDS has many features similar to autoimmune disease, including the hyperproduction of aberrant interferon, a type with little or no anti-HIV activity, protectively induced by HIV to allow its continued replication and survival. In other words, while most viruses induce normal IFN which protects the cells against viral infection, HIV induces an abnormal, defective kind of IFN which insures viral survival. The neutralization of hyperproduced interferons by polyclonal or monoclonal antibody produced in mouse, or preferably, human hybridoma, removal via

Phillip Gamble
1644 12/02

Record Date Created: 19941109
Record Date Completed: 19941109

QR185.8.L93L95

----------anti-tnf or anti-ifn hiv / aids ----------

0007651711 BIOSIS NO.: 199191034602
INCREASED HUMAN IMMUNODEFICIENCY VIRUS HIV EXPRESSION IN CHRONICALLY INFECTED U937 CELLS UPON IN-VITRO DIFFERENTIATION BY HYDROXYVITAMIN D3 ROLES OF INTERFERON AND TUMOR NECROSIS FACTOR IN REGULATION OF HIV PRODUCTION
AUTHOR: LOCARDI C (Reprint); PETRINI C; BOCCOLI G; TESTA U; DIEFFENBACH C; BUTTO S; BELARDELLI F
AUTHOR ADDRESS: LAB OF VIROL, IST SUPERIORE DI SANITA, VIALE REGINA ELENA, 299, 00161 ROME, ITALY**ITALY
JOURNAL: Journal of Virology 64 (12): p5874-5882 1990
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We have investigated the roles of cytokines in the modulation of human immunodeficiency virus (HIV) production in chronically infected U937 cells upon in vitro differentiation by hydroxyvitamin D3. HIV-infected U937 cells exhibited markedly lower levels of CD4 and HLA-DR antigens than uninfected cells did. Vitamin D3 induced a time-dependent macrophagelike differentiation, as determined by monitoring the expression of some surface antigens by means of the monoclonal antibodies OKM1, OKM5, OKM13, OKM14, OKT4, anti-HLA-DR, TecMG2, TecMG3, LeuM3, LeuM1, anti-HLA-DP, and anti-HLA-DQ. Treatment with hydroxyvitamin D3 resulted in a marked increase in HIV production compared with control cultures. Interleukin 1.beta. (IL-1.beta.) and tumor necrosis factor .alpha. (TNF-.alpha.) were detected in the culture media, whereas interferon (IFN) was not generally found. Using the polymerase chain reaction technique, we found HIV -infected U937 cells to express detectable levels of mRNAs for alpha interferon (IFN-.alpha.), IFN-.beta., TNF-.alpha. and IL-1.beta.. The addition of TNF resulted in a marked increase of HIV production, whereas IL-1.beta. was ineffective. In contrast, both IFN-.alpha. and IFN-.beta. exerted some inhibitory effect on HIV production, which was more marked in vitamin D3-treated cutlures than in untreated cultures. HIV production was significantly increased by antibodies to IFN-.alpha. in both untreated and vitamin 3-treated cultures. Anti-IFN-.beta. antibody increased HIV production only in vitamin D3-treated cells. In contrast, anti-TNF-.alpha. antibodies markedly decreased HIV production in both control and differentiating U937 cells. Vitamin D3 treatment resulted in a higher expression of TNF receptors in differentiating cells than in control HIV-infected cells. These data demonstrate a strong correlation between HIV production and macrophagelike differentiation in chronically infected U937 cells and suggest that endogenous IFN and TNF exert opposite effects in the regulation of virus production in both undifferentiated and vitamin D3-treated cell cultures.

Phillip Kemled 118 1644

----------anti-tnf or anti-ifn hiv / aids ----------

3/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008406813 BIOSIS NO.: 199294108654
THE IMMUNOMODULATORY ROLE OF IFN-ALPHA OR MALTOSE-STABILIZED IFN-ALPHA ON T-CELL ACTIVATION
AUTHOR: KOHNO K (Reprint); HOLAN V; MATSUDA S; KURIMOTO M; MINOWADA J
AUTHOR ADDRESS: FUJISAKI CELL CENT, HAYASHIBARA BIOCHEM LAB, INC, 675-1 FUJISAKI OKAYAMA 702, JPN**JAPAN
JOURNAL: Lymphokine and Cytokine Research 11 (4): p221-~~227~~ 1992 231
ISSN: 1056-5477

Record Date Created: 19941109
Record Date Completed: 19941109

QR355.V65

----------anti-tnf or anti-ifn hiv / aids ----------

0007651711 BIOSIS NO.: 199191034602
INCREASED HUMAN IMMUNODEFICIENCY VIRUS HIV EXPRESSION IN CHRONICALLY INFECTED U937 CELLS UPON IN-VITRO DIFFERENTIATION BY HYDROXYVITAMIN D3 ROLES OF INTERFERON AND TUMOR NECROSIS FACTOR IN REGULATION OF HIV PRODUCTION
AUTHOR: LOCARDI C (Reprint); PETRINI C; BOCCOLI G; TESTA U; DIEFFENBACH C; BUTTO S; BELARDELLI F
AUTHOR ADDRESS: LAB OF VIROL, IST SUPERIORE DI SANITA, VIALE REGINA ELENA, 299, 00161 ROME, ITALY**ITALY
JOURNAL: Journal of Virology 64 (12): p5874-5882 1990
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We have investigated the roles of cytokines in the modulation of human immunodeficiency virus (HIV) production in chronically infected U937 cells upon in vitro differentiation by hydroxyvitamin D3. HIV-infected U937 cells exhibited markedly lower levels of CD4 and HLA-DR antigens than uninfected cells did. Vitamin D3 induced a time-dependent macrophagelike differentiation, as determined by monitoring the expression of some surface antigens by means of the monoclonal antibodies OKM1, OKM5, OKM13, OKM14, OKT4, anti-HLA-DR, TecMG2, TecMG3, LeuM3, LeuM1, anti-HLA-DP, and anti-HLA-DQ. Treatment with hydroxyvitamin D3 resulted in a marked increase in HIV production compared with control cultures. Interleukin 1.beta. (IL-1.beta.) and tumor necrosis factor .alpha. (TNF-.alpha.) were detected in the culture media, whereas interferon (IFN) was not generally found. Using the polymerase chain reaction technique, we found HIV -infected U937 cells to express detectable levels of mRNAs for alpha interferon (IFN-.alpha.), IFN-.beta., TNF-.alpha. and IL-1.beta.. The addition of TNF resulted in a marked increase of HIV production, whereas IL-1.beta. was ineffective. In contrast, both IFN-.alpha. and IFN-.beta. exerted some inhibitory effect on HIV production, which was more marked in vitamin D3-treated cutlures than in untreated cultures. HIV production was significantly increased by antibodies to IFN-.alpha. in both untreated and vitamin 3-treated cultures. Anti-IFN-.beta. antibody increased HIV production only in vitamin D3-treated cells. In contrast, anti-TNF-.alpha. antibodies markedly decreased HIV production in both control and differentiating U937 cells. Vitamin D3 treatment resulted in a higher expression of TNF receptors in differentiating cells than in control HIV-infected cells. These data demonstrate a strong correlation between HIV production and macrophagelike differentiation in chronically infected U937 cells and suggest that endogenous IFN and TNF exert opposite effects in the regulation of virus production in both undifferentiated and vitamin D3-treated cell cultures.

Phillip Kombl 1644 118

----------anti-tnf or anti-ifn hiv / aids ----------

3/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008406813 BIOSIS NO.: 199294108654
THE IMMUNOMODULATORY ROLE OF IFN-ALPHA OR MALTOSE-STABILIZED IFN-ALPHA ON T-CELL ACTIVATION
AUTHOR: KOHNO K (Reprint); HOLAN V; MATSUDA S; KURIMOTO M; MINOWADA J
AUTHOR ADDRESS: FUJISAKI CELL CENT, HAYASHIBARA BIOCHEM LAB, INC, 675-1 FUJISAKI OKAYAMA 702, JPN**JAPAN
JOURNAL: Lymphokine and Cytokine Research 11 (4): p221-227 1992
ISSN: 1056-5477

Au: Walker, Robert E.

AUTHOR ADDRESS: LIR/NIAID, Build 10, Room 11C103, Bethesda, MD 20892, USA**
USA
JOURNAL: Journal of Infectious Diseases 174 (1): p63-68 1996 1996
ISSN: 0022-1899
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Tumor necrosis factor-alpha (TNF-alpha), a proinflammatory cytokine known to stimulate human immunodeficiency virus type I (HIV-1) replication, has been implicated in the pathogenesis of HIV-1 infection. Inhibition of TNF-alpha by a chimeric humanized monoclonal antibody, cA2, was investigated in 6 HIV-1-infected patients with CD4 cell counts lt 200/mm-3. Two consecutive infusions of 10 mg/kg 14 days apart were well tolerated, and a prolonged serum half-life for cA2 (mean, 257 +- 70 h) was demonstrated. Serum immunoreactive TNF-alpha concentrations fell from a mean prestudy value of 6.4 pg/mL (range, 4.2-7.9) to 1.1 pg/mL (range, 0.5-2.2) 24 h after the first infusion and returned to baseline within 7-14 days. A similar response was seen after the second infusion. No consistent changes in CD4 cell counts or plasma HIV RNA levels were observed over 42 days. Future studies evaluating the therapeutic utility of long-term TNF-alpha suppression using anti-TNF-alpha antibodies are feasible and warranted.

476388

6/7/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012878937 BIOSIS NO.: 200100050776
Activation of signal transduction and apoptosis in healthy lymphomonocytes exposed to bystander HIV-1-infected cells
AUTHOR: Abbate I; Dianzani F; Capobianchi M R (Reprint)
AUTHOR ADDRESS: Laboratory of Virology, National Institute for Infectious Diseases 'L. Spallanzani' I. R. C. C. S., Via Portuense, 292-00149, Rome, Italy**Italy
JOURNAL: Clinical and Experimental Immunology 122 (3): p374-380 December, 2000 2000
MEDIUM: print
ISSN: 0009-9104
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Persistent activation of the immune system is one of the hallmarks of HIV-1 infection. In this study we analysed the induction of factors involved in cytokine signal transduction, such as STAT 1 proteins and IRF-1 mRNA, in normal peripheral blood mononuclear cells (PBMC) exposed to HIV-infected cells, and the induction of apoptosis. Western blot analyses and reverse transcriptase-polymerase chain reaction results indicate that both cells infected with a X4 strain and cells infected with a R5 strain are able to increase intracellular levels of STAT 1alpha and beta proteins as well as IRF-1 mRNA. This effect was prevented by neutralizing antibodies against interferon-alpha (IFN-alpha). HIV-1-infected cells dose-dependently induced apoptotic commitment in normal PBMC, as revealed by DNA fragmentation analysis, but this was not accompanied by an increase of caspase-3 activity, even if a slight up-regulation of IL-1beta-converting enzyme mRNA was detected. Apoptosis induction could be abrogated mainly by antibodies against tumour necrosis factor-alpha (TNF-alpha) and, to a lesser extent, by antibodies against IFN-gamma. All these findings suggest that uninfected PBMC can undergo activation of signal transduction and apoptosis after exposure to bystander HIV-infected cells, subsequent to the induction of cytokines such as IFNs and TNF-alpha.

0012995027 BIOSIS NO.: 200100166866
Autoantibodies to TNFalpha in HIV-1 infection: Prospects for anti-cytokine vaccine therapy

105

AUTHOR: MATSUYAMA T (Reprint); HAMAMOTO Y; YOSHIDA T; KIDO Y; KOBAYASHI S; KOBAYASHI N; YAMAMOTO N
AUTHOR ADDRESS: DEP VIROL PARASITOLOGY, YAMAGUCHI UNIV SCH MED, 1144 KOGUSHI, UBE, YAMAGUCHI 755**JAPAN
JOURNAL: Japanese Journal of Cancer Research 79 (2): p156-159 1988
ISSN: 0910-5050
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

4446387

mw only

ABSTRACT: The effect of culture supernatant of MT-2 cells on human immunodeficiency virus (HIV)-producing cells. MOLT-4/HIVHTLV-IIIB cells, was examined. As compared to the effect on MOLT-4 cells, parent cells not infected with HIV, a selective cytotoxic/cytostatic effect on MOLT-4/HIVHTLV-IIIB cells was observed 4 days after treatment with up to 640-fold-diluted MT-2 supernatant. Furthermore, under similar conditions, a 2- to 6-fold increase in the number of HIV particles was detected in the culture of MOLT-4/HIVHTLV-IIIB cells 6 hr after treatment. Complete blocking of these effects by anti-lymphotoxin monoclonal antibody, but not by anti-tumor necrosis factor antibody, indicates that these effects of MT-2 supernatant on MOLT-4/HIVHTLV-IIIB cells are attributable to a lymphotoxin-related cytotoxic factor.

skurkovich ----------

8/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012878937 BIOSIS NO.: 200100050776
Activation of signal transduction and apoptosis in healthy lymphomonocytes exposed to bystander HIV-1-infected cells
AUTHOR: Abbate I; Dianzani F; Capobianchi M R (Reprint)
AUTHOR ADDRESS: Laboratory of Virology, National Institute for Infectious Diseases 'L. Spallanzani' I. R. C. C. S., Via Portuense, 292-00149, Rome, Italy**Italy
JOURNAL: Clinical and Experimental Immunology 122 (3): p374-380 December, 2000 2000
MEDIUM: print
ISSN: 0009-9104
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

#

ABSTRACT: Persistent activation of the immune system is one of the hallmarks of HIV-1 infection. In this study we analysed the induction of factors involved in cytokine signal transduction, such as STAT 1 proteins and IRF-1 mRNA, in normal peripheral blood mononuclear cells (PBMC) exposed to HIV-infected cells, and the induction of apoptosis. Western blot analyses and reverse transcriptase-polymerase chain reaction results indicate that both cells infected with a X4 strain and cells infected with a R5 strain are able to increase intracellular levels of STAT 1alpha and beta proteins as well as IRF-1 mRNA. This effect was prevented by neutralizing antibodies against interferon-alpha (IFN-alpha). HIV-1-infected cells dose-dependently induced apoptotic commitment in normal PBMC, as revealed by DNA fragmentation analysis, but this was not accompanied by an increase of caspase-3 activity, even if a slight up-regulation of IL-1beta-converting enzyme mRNA was detected. Apoptosis induction could be abrogated mainly by antibodies against tumour necrosis factor-alpha (TNF-alpha) and, to a lesser extent, by antibodies against IFN-gamma. All these findings suggest that uninfected PBMC can undergo activation of signal transduction and apoptosis after exposure to bystander HIV-infected cells, subsequent to the induction of cytokines such as IFNs and TNF-alpha.

skurkovich ----------

4/7/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

P Kelley 1644 Kimball 12/22

AUTHOR: Capini C J; Richardson M W; Hendel H; Sverstiuk A; Mirchandani J; Regulier E G; Khalili K; Zagury J F; Rappaport J (Reprint)
AUTHOR ADDRESS: Center for Neurovirology and Cancer Biology, Temple University, 1900 N. 12th St., Rm 246, Philadelphia, PA, 19122, USA**USA
JOURNAL: Biomedicine and Pharmacotherapy 55 (1): p23-31 February, 2001 2001
MEDIUM: print
ISSN: 0753-3322
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Tumor necrosis factor alpha (TNFalpha) is a proinflammatory cytokine principally involved in the activation of lymphocytes in response to viral infection. TNFalpha also stimulates the production of other cytokines, activates NK cells and potentiates cell death and/or lysis in certain models of viral infection. Although TNFalpha might be expected to be a protective component of an antiviral immune response, several lines of evidence suggest that TNFalpha and other virally-induced cytokines actually may contribute to the pathogenesis of HIV infection. Based on the activation of HIV replication in response to TNFalpha, HIV appears to have evolved to take advantage of host cytokine activation pathways. Antibodies to TNFalpha are present in the serum of normal individuals as well as in certain autoimmune disorders, and may modulate disease progression in the setting of HIV infection. We examined TNFalpha-specific antibodies in HIV-infected non-progressors and healthy seronegatives; anti-TNFalpha antibody levels are significantly higher in GRIV seropositive slow/non-progressors (N = 120, mean = 0.24), compared to seronegative controls (N = 12, mean = 0.11). TNFalpha antibodies correlated positively with viral load, (P = 0.013, r = 0.282), and CD8+ cell count (P = 0.03, r = 0.258), and inversely with CD4+ cell count (P = 0.003, r = -0.246), percent CD4+ cells (P = 0.008, r = -0.306), and CD4 :CD8 ratio (P = 0.033, r = -0.251). TNFalpha antibodies also correlated positively with antibodies to peptides corresponding to the CD4 binding site of gp160 (P = 0.001, r = 0.384), the CD4 identity region (P = 0.016, r = 0.29), the V3 loop (P = 0.005, r = 0.34), and the amino terminus of Tat (P = 0.001, r = 0.395); TNFalpha antibodies also correlated positively with antibodies to Nef protein (P = 0.008, r = 0.302). The production of anti-TNFalpha antibodies appears to be an adaptive response to HIV infection and suggests the potential utility of modified cytokine vaccines in the treatment of HIV infections as well as AIDS-related and unrelated autoimmune and CNS disorders.

6/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014049558 BIOSIS NO.: 200300008277
Elevated levels of tumor necrosis factor alpha (TNF-alpha) in human immunodeficiency virus type 1-transgenic mice: Prevention of death by antibody to TNF-alpha.
AUTHOR: De Swapan K; Devadas Krishnakumar; Notkins Abner Louis (Reprint)
AUTHOR ADDRESS: Experimental Medicine Section, Oral Immunity and Infection Branch, NIDCR, National Institutes of Health, 30 Convent Dr., Building 30, Room 121, MSC 4322, Bethesda, MD, 20892-4322, USA**USA
AUTHOR E-MAIL ADDRESS: anotkins@dir.nidcr.nih.gov
JOURNAL: Journal of Virology 76 (22): p11710-11714 November 2002 2002
MEDIUM: print
ISSN: 0022-538X _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Homozygous human immunodeficiency virus type 1 (HIV-1)-transgenic mice (Tg26) appear normal at birth but die within 3 to 4 weeks. The skin of these animals shows diffuse scaling and high-level expression of both HIV-1 mRNA and gp120. Previous experiments showed that treatment with human chorionic gonadatropin (hCG) prevented death and the expression of HIV-1 mRNA and gp120. The present

Att: Walker, Robert E.

AUTHOR ADDRESS: LIR/NIAID, Build 10, Room 11C103, Bethesda, MD 20892, USA** USA
JOURNAL: Journal of Infectious Diseases 174 (1): p63-68 1996 1996
ISSN: 0022-1899
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Tumor necrosis factor-alpha (TNF-alpha), a proinflammatory cytokine known to stimulate human immunodeficiency virus type I (HIV-1) replication, has been implicated in the pathogenesis of HIV-1 infection. Inhibition of TNF-alpha by a chimeric humanized monoclonal antibody, cA2, was investigated in 6 HIV-1-infected patients with CD4 cell counts lt 200/mm-3. Two consecutive infusions of 10 mg/kg 14 days apart were well tolerated, and a prolonged serum half-life for cA2 (mean, 257 +- 70 h) was demonstrated. Serum immunoreactive TNF-alpha concentrations fell from a mean prestudy value of 6.4 pg/mL (range, 4.2-7.9) to 1.1 pg/mL (range, 0.5-2.2) 24 h after the first infusion and returned to baseline within 7-14 days. A similar response was seen after the second infusion. No consistent changes in CD4 cell counts or plasma HIV RNA levels were observed over 42 days. Future studies evaluating the therapeutic utility of long-term TNF-alpha suppression using anti-TNF-alpha antibodies are feasible and warranted.

6/7/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

0012878937 BIOSIS NO.: 200100050776
Activation of signal transduction and apoptosis in healthy lymphomonocytes exposed to bystander HIV-1-infected cells
AUTHOR: Abbate I; Dianzani F; Capobianchi M R (Reprint)
AUTHOR ADDRESS: Laboratory of Virology, National Institute for Infectious Diseases 'L. Spallanzani' I. R. C. C. S., Via Portuense, 292-00149, Rome, Italy**Italy
JOURNAL: Clinical and Experimental Immunology 122 (3): p374-380 December, 2000 2000
MEDIUM: print
ISSN: 0009-9104
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Persistent activation of the immune system is one of the hallmarks of HIV-1 infection. In this study we analysed the induction of factors involved in cytokine signal transduction, such as STAT 1 proteins and IRF-1 mRNA, in normal peripheral blood mononuclear cells (PBMC) exposed to HIV-infected cells, and the induction of apoptosis. Western blot analyses and reverse transcriptase-polymerase chain reaction results indicate that both cells infected with a X4 strain and cells infected with a R5 strain are able to increase intracellular levels of STAT 1alpha and beta proteins as well as IRF-1 mRNA. This effect was prevented by neutralizing antibodies against interferon-alpha (IFN-alpha). HIV-1-infected cells dose-dependently induced apoptotic commitment in normal PBMC, as revealed by DNA fragmentation analysis, but this was not accompanied by an increase of caspase-3 activity, even if a slight up-regulation of IL-1beta-converting enzyme mRNA was detected. Apoptosis induction could be abrogated mainly by antibodies against tumour necrosis factor-alpha (TNF-alpha) and, to a lesser extent, by antibodies against IFN-gamma. All these findings suggest that uninfected PBMC can undergo activation of signal transduction and apoptosis after exposure to bystander HIV-infected cells, subsequent to the induction of cytokines such as IFNs and TNF-alpha.

0012995027 BIOSIS NO.: 200100166866
Autoantibodies to TNFalpha in HIV-1 infection: Prospects for anti-cytokine vaccine therapy

Phillip Dambl
1644 12/22

AUTHOR: MATSUYAMA T (Reprint); HAMAMOTO Y; YOSHIDA T; KIDO Y; KOBAYASHI S; KOBAYASHI N; YAMAMOTO N
AUTHOR ADDRESS: DEP VIROL PARASITOLOGY, YAMAGUCHI UNIV SCH MED, 1144 KOGUSHI, UBE, YAMAGUCHI 755**JAPAN
JOURNAL: Japanese Journal of Cancer Research 79 (2): p156-159 1988
ISSN: 0910-5050
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effect of culture supernatant of MT-2 cells on human immunodeficiency virus (HIV)-producing cells. MOLT-4/HIVHTLV-IIIB cells, was examined. As compared to the effect on MOLT-4 cells, parent cells not infected with HIV, a selective cytotoxic/cytostatic effect on MOLT-4/HIVHTLV-IIIB cells was observed 4 days after treatment with up to 640-fold-diluted MT-2 supernatant. Furthermore, under similar conditions, a 2- to 6-fold increase in the number of HIV particles was detected in the culture of MOLT-4/HIVHTLV-IIIB cells 6 hr after treatment. Complete blocking of these effects by anti-lymphotoxin monoclonal antibody, but not by anti-tumor necrosis factor antibody, indicates that these effects of MT-2 supernatant on MOLT-4/HIVHTLV-IIIB cells are attributable to a lymphotoxin-related cytotoxic factor.

skurkovich ----------

8/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012878937 BIOSIS NO.: 200100050776
Activation of signal transduction and apoptosis in healthy lymphomonocytes exposed to bystander HIV-1-infected cells
AUTHOR: Abbate I; Dianzani F; Capobianchi M R (Reprint)
AUTHOR ADDRESS: Laboratory of Virology, National Institute for Infectious Diseases 'L. Spallanzani' I. R. C. C. S., Via Portuense, 292-00149, Rome, Italy**Italy
JOURNAL: Clinical and Experimental Immunology 122 (3): p374-380 December, 2000 2000
MEDIUM: print
ISSN: 0009-9104
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Persistent activation of the immune system is one of the hallmarks of HIV-1 infection. In this study we analysed the induction of factors involved in cytokine signal transduction, such as STAT 1 proteins and IRF-1 mRNA, in normal peripheral blood mononuclear cells (PBMC) exposed to HIV-infected cells, and the induction of apoptosis. Western blot analyses and reverse transcriptase-polymerase chain reaction results indicate that both cells infected with a X4 strain and cells infected with a R5 strain are able to increase intracellular levels of STAT 1alpha and beta proteins as well as IRF-1 mRNA. This effect was prevented by neutralizing antibodies against interferon-alpha (IFN-alpha). HIV-1-infected cells dose-dependently induced apoptotic commitment in normal PBMC, as revealed by DNA fragmentation analysis, but this was not accompanied by an increase of caspase-3 activity, even if a slight up-regulation of IL-1beta-converting enzyme mRNA was detected. Apoptosis induction could be abrogated mainly by antibodies against tumour necrosis factor-alpha (TNF-alpha) and, to a lesser extent, by antibodies against IFN-gamma. All these findings suggest that uninfected PBMC can undergo activation of signal transduction and apoptosis after exposure to bystander HIV-infected cells, subsequent to the induction of cytokines such as IFNs and TNF-alpha.

skurkovich ----------

4/7/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

22.00

AUTHOR: Capini C J; Richardson M W; Hendel H; Sverstiuk A; Mirchandani J; Regulier E G; Khalili K; Zagury J F; Rappaport J (Reprint)
AUTHOR ADDRESS: Center for Neurovirology and Cancer Biology, Temple University, 1900 N. 12th St., Rm 246, Philadelphia, PA, 19122, USA**USA
JOURNAL: Biomedicine and Pharmacotherapy 55 (1): p23-31 February, 2001 2001
MEDIUM: print
ISSN: 0753-3322
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

Abstracts only

ABSTRACT: Tumor necrosis factor alpha (TNFalpha) is a proinflammatory cytokine principally involved in the activation of lymphocytes in response to viral infection. TNFalpha also stimulates the production of other cytokines, activates NK cells and potentiates cell death and/or lysis in certain models of viral infection. Although TNFalpha might be expected to be a protective component of an antiviral immune response, several lines of evidence suggest that TNFalpha and other virally-induced cytokines actually may contribute to the pathogenesis of HIV infection. Based on the activation of HIV replication in response to TNFalpha, HIV appears to have evolved to take advantage of host cytokine activation pathways. Antibodies to TNFalpha are present in the serum of normal individuals as well as in certain autoimmune disorders, and may modulate disease progression in the setting of HIV infection. We examined TNFalpha-specific antibodies in HIV-infected non-progressors and healthy seronegatives; anti-TNFalpha antibody levels are significantly higher in GRIV seropositive slow/non-progressors (N = 120, mean = 0.24), compared to seronegative controls (N = 12, mean = 0.11). TNFalpha antibodies correlated positively with viral load, (P = 0.013, r = 0.282), and CD8+ cell count (P = 0.03, r = 0.258), and inversely with CD4+ cell count (P = 0.003, r = -0.246), percent CD4+ cells (P = 0.008, r = -0.306), and CD4 :CD8 ratio (P = 0.033, r = -0.251). TNFalpha antibodies also correlated positively with antibodies to peptides corresponding to the CD4 binding site of gp160 (P = 0.001, r = 0.384), the CD4 identity region (P = 0.016, r = 0.29), the V3 loop (P = 0.005, r = 0.34), and the amino terminus of Tat (P = 0.001, r = 0.395); TNFalpha antibodies also correlated positively with antibodies to Nef protein (P = 0.008, r = 0.302). The production of anti-TNFalpha antibodies appears to be an adaptive response to HIV infection and suggests the potential utility of modified cytokine vaccines in the treatment of HIV infections as well as AIDS-related and unrelated autoimmune and CNS disorders.

Phillip Hendel
1644 12/22

6/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014049558 BIOSIS NO.: 200300008277
Elevated levels of tumor necrosis factor alpha (TNF-alpha) in human immunodeficiency virus type 1-transgenic mice: Prevention of death by antibody to TNF-alpha.
AUTHOR: De Swapan K; Devadas Krishnakumar; Notkins Abner Louis (Reprint)
AUTHOR ADDRESS: Experimental Medicine Section, Oral Immunity and Infection Branch, NIDCR, National Institutes of Health, 30 Convent Dr., Building 30, Room 121, MSC 4322, Bethesda, MD, 20892-4322, USA**USA
AUTHOR E-MAIL ADDRESS: anotkins@dir.nidcr.nih.gov
JOURNAL: Journal of Virology 76 (22): p11710-11714 November 2002 2002
MEDIUM: print
ISSN: 0022-538X _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Homozygous human immunodeficiency virus type 1 (HIV-1)-transgenic mice (Tg26) appear normal at birth but die within 3 to 4 weeks. The skin of these animals shows diffuse scaling and high-level expression of both HIV-1 mRNA and gp120. Previous experiments showed that treatment with human chorionic gonadatropin (hCG) prevented death and the expression of HIV-1 mRNA and gp120. The present